

What Is the Added Benefit of Oropharyngeal Swabs Compared to Nasal Swabs Alone for Respiratory Virus Detection in Hospitalized Children Aged <10 Years?

Fatimah S. Dawood,¹ Jorge Jara,³ Dora Estripeaut,⁴ Ofelina Vergara,⁴ Kathia Luciani,⁵ Mary Corro,⁵ Tirza de León,⁷ Ricardo Saldaña,⁷ Juan Miguel Castillo Baires,⁸ Rafael Rauda Flores,⁸ Rafael A. Cazares,⁹ Yarisá Sujey Brizuela de Fuentes,⁹ Danilo Franco,⁶ Melissa Gaitan,⁶ Eileen Schneider,² LaShondra Berman,¹ Eduardo Azziz-Baumgartner,¹ and Marc-Alain Widdowson¹

¹Influenza Division, and ²Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; ³Centro de Estudios en Salud, Universidad del Valle de Guatemala, Guatemala City; ⁴Hospital Del Niño, ⁵Hospital De Especialidades Pediátricas Omar Torrijos, ⁶Gorgas Memorial Institute for Health Studies, Panama City, and ⁷Hospital Materno Infantil José Domingo De Obaldía, David, Panama; ⁸Hospital San Juan De Dios, Santa Ana, and ⁹Hospital San Juan De Dios, San Miguel, El Salvador

We evaluated the added value of collecting both nasal and oropharyngeal swabs, compared with collection of nasal swabs alone, for detection of common respiratory viruses by reverse transcription–polymerase chain reaction in hospitalized children aged <10 years. Nasal swabs had equal or greater sensitivity than oropharyngeal swabs for detection of respiratory syncytial virus, adenovirus, human metapneumovirus, rhinovirus, and influenza virus but not parainfluenza virus. The addition of an oropharyngeal swab, compared with use of a nasal swab alone, increased the frequency of detection of each respiratory virus by no more than 10% in children aged <10 years.

Keywords. influenza, human; respiratory syncytial virus infections; parainfluenza; human metapneumovirus; children, hospitalized.

The advent and increased availability of polymerase chain reaction (PCR) for the detection of common respiratory viruses has led to increased recognition of respiratory viruses as important

contributors to severe respiratory illness. Although PCR is highly sensitive, compared with viral culture, for detection of many respiratory viruses, specimen type is an important factor that affects test sensitivity. Currently, a variety of respiratory specimen types are routinely used for diagnostic and surveillance purposes, including nasopharyngeal (NP) aspirates or washes and NP, mid-turbinate, nasal, or oropharyngeal (OP) swab. Collection of NP specimens may involve considerable discomfort for patients and requires more-technical experience on the part of specimen collectors, whereas nasal and OP swabs are less invasive and thus likely to be more acceptable, particularly to parents of young children. As a result, paired nasal and OP swabs are frequently collected for clinical diagnosis and surveillance of respiratory virus infections in children.

Prior studies of test performance for respiratory virus detection have shown that the sensitivities of NP swabs in adults [1] and NP aspirates in children [2, 3] are comparable to that of nasal swabs for most viruses and that NP swabs are generally more sensitive than OP swabs [4–7]. However, the performance of nasal swabs versus OP swabs for respiratory virus detection has not been evaluated. Collection of a single respiratory specimen, rather than paired specimens from 2 sources, is more efficient and might further increase the acceptability of specimen collection in children. Therefore, we used data from a randomized, controlled trial that enrolled children aged <10 years hospitalized with respiratory illness in which nasal and OP swabs were collected separately to evaluate their sensitivities for detection of 6 common respiratory viruses and the added benefit of obtaining an OP swab plus nasal swab rather than a nasal swab alone.

METHODS

OP and nasal swabs were collected as part of a multisite prospective, randomized, placebo-controlled trial of the efficacy of oseltamivir treatment, conducted in 2012 and 2013. Study sites included tertiary care hospitals in Panama (3 hospitals) and El Salvador (2 hospitals). Participants were enrolled during September–October 2012 and April–October 2013. To be eligible for enrollment, children had to be aged <10 years and hospitalized <7 days after symptom onset with respiratory illness, defined as cough or sore throat plus age-specific tachypnea.

OP and nasal swabs were collected from each participant at the time of enrollment, prior to administration of oseltamivir or placebo. Intubated patients (n = 6) had endotracheal aspirates collected in lieu of throat swabs and were not included in this analysis. Study physicians were trained to collect nasal and

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Correspondence: Fatimah S. Dawood, MD, Influenza Division, Centers for Disease Control and Prevention, 1600 Clifton Rd, MS A-32, Atlanta, GA 30329 (fdawood@cdc.gov).

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throat swabs by using standard guidelines and underwent periodic quality checks to ensure adherence to guidelines. Dacron-flocked swabs were used for collection of nasal and OP swabs. Nasal swabs were collected by inserting the swab into a single nostril and rubbing the swab against the nasal septum for 2–3 seconds. OP swabs were collected by inserting the swab into the posterior OP and rubbing the swab against both tonsils for 2–3 seconds. Nasal and OP swabs were placed immediately into separate vials of 3 mL of universal transport medium (Copan Diagnostics), stored at 4°C at the hospital for no more than 72 hours, and transported to the national reference laboratory for processing. All specimens were tested at the Gorgas Memorial Institute for Health Studies by singleplex real-time reverse transcription–PCR (RT-PCR) for respiratory syncytial virus (RSV), parainfluenza viruses 1–3, adenovirus, human metapneumovirus (hMPV), rhinovirus, and influenza virus, including influenza B virus, influenza A(H1N1)pdm09 virus, and influenza A(H3N2) virus, using Centers for Disease Control and Prevention protocols (available upon request) [6]. Real-time RT-PCR threshold cycle (Ct) values, a fluorescent signal detected above the threshold value, were recorded for all positive test results. Ct values are inversely correlated with the amount of viral nucleic acid (ie, viral load) present in a sample.

The gold standard was defined as detection of a virus by either nasal or OP swab for each participant. The sensitivities of nasal swabs alone and OP swabs alone were calculated using the gold standard for comparison, and 95% confidence intervals (CIs) for sensitivity estimates were calculated using the continuity corrected score method [8]. The percentage increase in detection by the addition of an OP swab, compared with use of a nasal swab alone, was calculated as $1 - [\text{number positive by nasal swab}/\text{number positive by gold standard}]$. Differences in Ct values between positive nasal swabs, compared with positive

OP swabs, were calculated for each participant who had positive results for both swab types as a proxy for relative difference in the amount of virus present in the 2 specimen types.

RESULTS

During 2012–2013, 718 participants were enrolled, of whom 18 (2%) were excluded because they did not have paired nasal and OP swabs (17 of 18) or did not have the source of their specimens labeled (1 of 18). Of the 703 hospitalized children (64 in 2012 and 639 in 2013) with paired nasal and OP swabs obtained at admission, 416 (59%) were male, 361 (51%) were aged <1 year, 263 (37%) were aged 1–2 years, and 79 (11%) were aged >2 years. The median time from symptom onset to specimen collection was 3 days (interquartile range, 2–4 days). The majority of children had a history of cough (99%), rhinorrhea (88%), difficulty breathing (88%), and fever or feverishness (78%). Six children (1%) required intensive care unit admission, and 5 (1%) required mechanical ventilation.

Among hospitalized children, the most commonly detected viruses by either nasal or OP swab were RSV (49%) and rhinovirus (22%; Table 1). The sensitivity of nasal swabs was greater than or equal to that of OP swabs for detection of all viruses except parainfluenza virus. OP swabs were least sensitive for detection of rhinovirus (83%; 95% CI, 75%–88%) and influenza virus (83%; 95% CI, 65%–94%). The addition of an OP swab, compared with collection of a nasal swab alone, increased detection by 9% (95% CI, 3%–23%) for parainfluenza virus, 7% (0%–36%) for adenovirus, and 6% (95% CI, 3–11%) for rhinovirus. The addition of an OP swab did not increase detection of influenza virus, as the sensitivity of nasal swab for detection of influenza virus was 100% (95% CI, 86%–100%). Results were similar when children were stratified by age <1 year versus

Table 1. Sensitivity of Nasal Versus Oropharyngeal (OP) Swabs, Compared With Detection by Either Swab Type, Among 703 Children Hospitalized With Respiratory Illness

Virus	Positive Nasal or OP Swabs, Proportion (%)	Positive Nasal Swabs		Positive OP Swabs		Mean Ct Value ^a Difference Between Positive Nasal vs OP Swabs	Percentage Increase in Detection With OP Swabs (95% CI)
		No.	Sensitivity, % (95% CI)	No.	Sensitivity, % (95% CI)		
RSV	343/703 (49)	335	98 (95–99)	320	93 (90–96)	–3 (–19 to 16)	2 (1–5)
Rhinovirus	152/703 (22)	143	94 (89–97)	126	83 (76–88)	–1 (–12 to 12)	6 (3–11)
PIV 1–3	43/703 (6)	39	91 (77–97)	42	98 (86–100)	–2 (–10 to 6)	9 (3–23)
hMPV	42/703 (6)	41	98 (86–100)	39	93 (79–98)	–2 (–11 to 10)	2 (0–14)
Influenza virus	30/703 (4)	30	100 (86–100)	25	83 (65–94)	2 (0–5)	0 (0–14)
Adenovirus	14/639 ^b (2)	13	93 (64–100)	13	93 (64–100)	–3 (–14 to 2)	7 (0–36)

Abbreviations: CI, confidence interval; Ct, cycle threshold; hMPV, human metapneumovirus; PIV, parainfluenza virus; RSV, respiratory syncytial virus.

^a The Ct value is the number of polymerase chain reaction cycles necessary for a specimen to turn positive. Ct values are inversely correlated with the amount of nucleic acid (virus) present in the sample. Ct value difference between positive nasal and OP swabs was calculated for each participant as follows: [nasal swab Ct value] – [OP swab Ct value]. Means and ranges of Ct value differences are shown.

^b Only specimens collected during 2013 were tested for adenoviruses (n = 639).

≥ 1 year and by time from symptom onset of ≤ 2 days versus > 2 days (results not shown). Ct values for each participant were lower for positive nasal swabs, compared with OP swabs, for each virus type except influenza virus.

DISCUSSION

Using standardized specimen collection techniques, we found that nasal swabs had greater or equal sensitivity than OP swabs for RT-PCR-based detection of most common respiratory viruses. Comparison of Ct values for positive swabs suggested that viral loads also were similar or higher in nasal swabs, compared with OP swabs, for all viruses except influenza virus. The addition of an OP swab, compared with use of a nasal swab alone, increased detection of each respiratory virus in our study by no more than 10% and did not increase detection of influenza virus. Overall, our findings suggest that collection of nasal swabs alone may be adequate in most cases for surveillance and diagnosis in hospitalized children aged ≤ 2 years when RT-PCR is being used, although dual specimen collection may be warranted under certain circumstances. We are only able to draw conclusions about the utility of paired OP and nasal swabs, compared with nasal swabs alone, among children aged ≤ 2 years because only 11% of children in our study were aged > 2 years.

To our knowledge, this is the first study to compare nasal and OP swabs for respiratory virus detection in hospitalized children. Prior studies comparing NP aspirates to nasal swabs in hospitalized children have found no difference in sensitivity for most viruses [2, 3, 9], except RSV, for which one study found that NP aspirates had higher sensitivity [2]. Two prior studies comparing NP and OP swabs in hospitalized children produced mixed results, with one study showing that the addition of an OP swab increased detection by $> 10\%$ for RSV, parainfluenza virus, influenza virus, adenovirus and hMPV and the other showing increased detection only for parainfluenza virus and influenza virus [4, 6]. However, these studies used different swab types for collection of NP versus OP swabs, complicating the direct comparison of detection from each source.

A limitation of our study is the relatively small number of specimens positive for influenza virus, which precluded evaluation of specimen sensitivity by influenza virus type and subtype. Although a previously published study found differences in the sensitivity of NP versus OP swabs by influenza virus subtype [6], nasal swabs detected 100% of children with influenza in our study. Strengths of our study include the inclusion of > 700 children at 5 hospitals in 2 countries, use of standardized specimen collection methods by trained physicians, and use of a consistent swab type for both nasal and OP specimen collection, making direct comparison of specimen types easier to interpret.

Nasal swabs are the least invasive of all respiratory specimen techniques and require minimal technical skill for collection. Several studies have shown that nasal swab collection by self-swabbing in adults or by parents for children produces similar results to collection by trained study staff [10, 11]. In contrast, OP specimen collection is more challenging in young children and may require restraining an uncooperative child and use of tongue depressors to obtain an adequate sample. Our results suggest that collection of OP swabs in addition to nasal swabs in noncritically ill hospitalized children may have little added value, considering the added burden of patient discomfort, staff time, and swabbing supplies, particularly when infection with RSV, hMPV, or seasonal influenza virus is suspected. Our findings held true for infants aged < 1 year, from whom collection of OP swabs may be most difficult. However, collection of respiratory specimens from multiple sources, including the lower respiratory tract, may be warranted in critically ill children for diagnostic purposes. Collection of specimens from multiple sources may also be warranted in outbreaks and for surveillance of novel respiratory viruses for which the optimal specimen source may be unknown or when infection with parainfluenza virus or adenovirus is suspected.

Notes

Disclaimer. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention (CDC).

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